Abstract

Methods and reagents for the detection and selection of two interacting-polypeptides, especially integral membrane proteins and transcription factors, by monitoring the reassembly of ubiquitin amino-terminal and carboxy-terminal chimeric polypeptide fragments are disclosed. Negative selection against an N-end rule-labilized marker released following ubiquitin reassembly allows direct selection of the interacting polypeptide pair. Methods to identify agonists and antagonists for certain protein-protein interactions; methods and reagents/kits for identifying proteins that binds a target protein are also provided. The dynamic and adaptable nature of the assay allows adaptation to a number of applications - such as probing the molecular environment of cellular membrane proteins *in vivo*.